



## Therapeutic Class Review<sup>SM</sup>

### Ethinyl estradiol/Drospirenone (YAZ<sup>®</sup>)

September 2006

#### New Product for Review:

YAZ (1 x 28 day cycle) --

Contains: 24 active tablets of  
- 3 mg drospirenone  
- 20 mcg ethinyl estradiol (EE)  
4 inert tablets

#### Dossier Provided by Manufacturer: yes

#### Dossier Evaluation: 1

1- dossier w/missing components  
2- all components present, except pharmacoeconomic model  
3- all components present (comprehensive)

**Available Therapeutic Alternatives:** See tables 1 through 7, pages 4 – 7.

#### Reason for Review

Determine formulary status for drospirenone/EE (YAZ), a new monophasic combination oral contraceptive (COC) formulation containing ethinyl estradiol 20 mcg combined with 3 mg drospirenone and 4 tablets of inert tablets.

#### Executive Summary

##### General Considerations

- The FDA recognizes that all approved COCs represent the most reliable birth control methods with:
  - greater than 99% effectiveness if used correctly, taking the pills consistently, every day.
  - 95 % effectiveness with typical use.
- Despite generic equivalents that are available for approximately 90% of branded COCs, brand loyalty is high for this therapeutic class because of aggressive marketing and advertising.
- Health plans commonly maintain a comprehensive selection of branded formulary contraceptive products with the ultimate goal of offering:
  - A competitive formulary of contraceptives that attracts the healthy young female population (a sector generally viewed as primary healthcare decision makers).
  - Several contraceptive formulations that may meet a woman's specific and personal contraceptive needs.

#### Drospirenone/EE (YAZ)

- Drospirenone 3mg /EE 20mcg (YAZ) is the newest COC to market that contains 10 mcg EE less per pill than its predecessor drospirenone 3mg/EE 30mcg (Yasmin).

- Drospirenone/EE (YAZ) is promoted for its:
  - Unique progestin component, drospirenone that has antimineralocorticoid (similar to 25mg spironolactone) and antiandrogenic properties.
  - Effective contraception with three additional days of estrogen/progestin that may result in less hormonal fluctuation between cycles than traditional 21-day COCs.
  - Potential use in premenstrual dysphoric disorder (PMDD) (emotional and physical symptoms of PMS) and acne.

## Evidence

### *Preventing Pregnancy*

- The FDA recognizes uncontrolled, open-label trial designs to establish efficacy of COCs in preventing pregnancy. Factors they consider include:
  - The unethical practice of using a placebo comparator.
  - Currently available COC formulations containing similar ethinyl estradiol and progestin combinations already approved and used for contraception.
- Trials with drospirenone/EE (YAZ) use an uncontrolled study design, making it difficult to determine whether the results from the trial were due to treatment or unintended bias.
  - There is no useful evidence that drospirenone/EE (YAZ) provides a clinically relevant therapeutic advantage or disadvantages to currently available COCs.
  - There is no useful evidence that drospirenone/EE (YAZ) has a side-effect profile significantly different from currently available low dose COCs.
- There are no proven clinical advantages of efficacy, safety, or maintaining cycle control for drospirenone/EE (YAZ) compared to:
  - Other monophasic COCs
  - Biphasic or triphasic COCs
  - COCs with different progestins and/or doses.
    - Although different progestins may pharmacologically differ in progestogenic and androgenic potency, there is no useful evidence that different progestins (norethynodrel, norethindrone, ethynodiol acetate, levonorgestrel, desogestrel, norgestimate, drospirenone) confer additional benefits of efficacy or decreases overall harms/risks with COC use.
    - There is no evidence that the antimineralocorticoid activity with drospirenone provides additional health benefits.
  - COCs with different estrogen components equivalent to 20 – 50 mcg ethinyl estradiol per pill. (There is no evidence to show that further reductions in the estrogenic content to 20 mcg ethinyl estradiol confers any added benefit).
  - Regimens using a 21-, 24- or 84-day treatment cycles.

- Combination transdermal or vaginal ring contraceptives, such as OrthoEvra<sup>®</sup> or NuvaRing<sup>®</sup>.

### ***Non-contraceptive Health Benefits***

- The evidence for drospirenone/EE (YAZ) in treating:
  - PMDD is unreliable due to high rate of discontinuation.
  - Acne is not useful because of high drop-out rates and missing details to confirm validity of results.
- Caution is urged regarding uncertain evidence in making health care decisions.

### ***Safety***

- There is no reliable evidence that currently marketed COCs, including drospirenone/EE (YAZ) differ in potential harms.
  - All combination hormone products, regardless of route and estrogen/progestin doses, carry similar precautions, risks, contraindications, and blackbox warnings.
  - The side effect profile for drospirenone/EE (YAZ) is consistent to other available estrogen/progestin oral contraceptive products.
- There is no useful evidence to permit conclusions on differences between COCs for:
  - Risk of stroke in otherwise healthy young women < 35 years old, who use currently marketed COCs.
  - Differences in COCs and their effect on weight.
- FDA labeling notes concerns regarding:
  - Potential drug interactions with all COCs.
  - Cardiovascular risk that may increase among COC users who are over the age of 35 or who are heavy smokers (15 or more cigarettes per day).
  - Potential risks for hyperkalemia with YAZ in patients who have predisposing factors (i.e., renal insufficiency, hepatic dysfunction and adrenal insufficiency).
    - YAZ contains 3mg of drospirenone that has antimineralocorticoid activity.
    - The potential for hyperkalemia may be comparable to a 25 mg dose of spironolactone.

### ***Considerations in subpopulations:***

- Risk versus benefit considerations are necessary in special populations, such as women over 35 years age, smokers, perimenopausal women and adolescents.
  - Pediatrics: There is no useful evidence to establish the safety and efficacy in pediatric patients less than 16 years of age. Use before menarche is not indicated.
  - Geriatrics: There is no package labeling regarding this population. There is no useful evidence to establish that COC use for non-contraceptive health benefits to outweigh potential harms.
  - Race, ethnicity: Current clinical experience has not identified differences in safety or efficacy based on race or ethnicity.

## Conclusion

- Drospirenone/EE (YAZ) is non-formulary/non-preferred because there is no useful evidence that this product provides additional clinical value over existing combination contraceptive products for the prevention of pregnancy or other non-contraceptive health benefits.

## Products

**TABLE 1: PRODUCT FOR REVIEW**

| Drug Products                       | FDA approval <sup>a</sup> | FDA approved indications | Usual Dose/Route  | Cost <sup>b</sup> | Potential Off-label Uses*             |
|-------------------------------------|---------------------------|--------------------------|---|-------------------|---------------------------------------|
| EE/Drospirenone (YAZ <sup>®</sup> ) | 3/16/2006                 | Prevention of pregnancy  | 1 active tablet orally daily on days 1-24, followed by 1 inert tablet days 25-28. | \$49.94           | Premenstrual dysphoric disorder; Acne |

<sup>a</sup> Date applies to approval date for the original brand name medication where there are now generics available.

<sup>b</sup> Cost estimate based on AWP (average wholesale price) listed in First Data Bank as of June 2006 for 1 month of therapy.

\* Other non-contraceptive health benefits related to the use of oral contraceptives listed in package labeling, but are based on epidemiological studies which largely utilized oral-contraceptive formulations containing ethinyl estradiol doses exceeding those contained in YAZ (i.e. >0.035 mg). Other health benefits based on class labeling for oral contraceptives are 1) increased menstrual cycle regularity, 2) decreased blood loss and incidence of iron-deficiency anemia, 3) decreased incidence of dysmenorrhea, 4) decreased incidence of functional ovarian cysts, 4) decreased incidence of ectopic pregnancies, 5) decreased incidence of fibroadenomas and fibrocystic disease of the breast, 6) decreased incidence of acute pelvic inflammatory disease, 7) decreased incidence of endometrial cancer, and 8) decreased incidence of ovarian cancer.<sup>6</sup>

Note: Ortho-Tricyclen and Estrostep are two COCs that have FDA approved indications for acne.

**TABLE 2: MONOPHASIC ORAL CONTRACEPTIVES PRODUCTS (GROUPED BY GENERIC EQUIVALENCY)**

| Formulary | Medication Products (EE = ethinyl estradiol)  | Mfg              | AWP Cost per cycle <sup>a</sup> | MAC per cycle <sup>a</sup> |
|-----------|---|------------------|---------------------------------|----------------------------|
| Yes       | ALESSE <sup>®</sup> = levonorgestrel 0.1mg/ EE 20 mcg   | Wyeth            | \$40.84                         | \$21.56                    |
|           | LEVLITE <sup>®</sup> = levonorgestrel 0.1mg/EE 20 mcg   | Berlex           | \$38.85                         | \$21.56                    |
| Yes       | <b>Levonorgestrel/EE 20mcg</b> (AVIANE) AB-rated generic Alesse <sup>®</sup>  | Barr             | \$35.16                         | \$21.56                    |
| Yes       | <b>Levonorgestrel/EE 20 mcg</b> (LUTERA) AB-rated generic Alesse  | Watson           | \$35.16                         | \$21.56                    |
| Yes       | <b>Levonorgestrel/EE 20 mcg</b> (LESSINA) AB-rated generic Levlite  | Barr             | \$34.96                         | \$21.56                    |
| Yes       | <b>Levonorgestrel/EE 20 mcg</b> (SRONYX) AB-rated generic Levlite   | Watson           | \$35.16                         | \$21.56                    |
| Yes       | ORTHO-CEPT <sup>®</sup> = desogestrel 15mcg / EE 30 mcg   | Ortho            | \$55.33                         | \$21.28                    |
| Yes       | DESOGEN <sup>®</sup> = desogestrel 15 mcg / EE 30mcg  | Organon          | \$35.44                         | \$21.28                    |
| Yes       | <b>Desogestrel 15 mcg /EE 30 mcg</b> (APRI) AB-rated generic  | Barr             | \$30.52                         | \$21.28                    |
| Yes       | <b>Desogestrel 15 mcg /EE 30 mcg</b> (Reclipsen) AB-rated generic   | Watson           | \$39.35                         | \$21.28                    |
| Yes       | <b>Desogestrel/EE</b> (Solia) AB-rated generic  | Prasco Labs      | \$30.52                         | \$21.28                    |
| Yes       | ORTHO-CYCLEN <sup>®</sup> = norgestimate 0.25mg / EE 35mcg  | Ortho            | \$52.81                         | \$21.28                    |
| Yes       | <b>Norgestimate 0.25mg /EE 35 mcg</b> (MONONESSA)<br>(Note: Watson brand via supply agreement w/Ortho) – same as Ortho-Cyclen   | Watson           | \$34.10                         | \$21.28                    |
| Yes       | <b>Norgestimate 0.25mg / /EE 35 mcg</b> (SPRINTEC) AB-rated generic   | Barr             | \$32.23                         | \$21.28                    |
| Yes       | <b>Norgestimate 0.25mg /EE 35 mcg</b> (PREVIFEM) AB-rated generic   | Teva             | \$32.23                         | \$21.28                    |
|           | OVCON <sup>®</sup> = 0.4 norethindrone / 35mcg EE   | WC Prof Products | \$47.68                         | --                         |
| Yes       | MODICON <sup>®</sup> = 0.5 norethindrone /35 mcg EE   | Ortho            | \$60.35                         | \$23.80                    |
| Yes       | ORTHO-NOVUM <sup>®</sup> =<br>1mg norethindrone with 35mcg EE or mestranol 50mcg)   | Ortho            | \$55.33                         | \$22.40                    |
| Yes       | NORINYL <sup>®</sup> 1+35; 1+50 (AB-rated Brand of Ortho-Novum)<br>= 1 mg norethindrone + EE 35mcg<br>= 1 mg norethindrone + mestranol 50 mcg                                     | Watson           | \$50.35                         | \$22.40                    |
| Yes       | <b>Norethindrone/EE</b> (NECON)<br>AB-rated generic to Modicon <sup>®</sup> 0.5 mg norethindrone/35mcg EE<br>AB-rated generic Ortho-Novum <sup>®</sup> 1mg norethindrone/35mcg EE | Watson           | \$32.14<br>\$29.47              | \$23.80<br>\$21.00         |
| Yes       | <b>Norethindrone/EE</b> (NORTREL) generic<br>0.5mg norethindrone/35mcg EE - AB-rated to Modicon <sup>®</sup><br>1mg/35mcg EE - AB-rated to Ortho-Novum <sup>®</sup> 1/35          | Barr             | \$32.17<br>\$29.50              | \$23.80<br>\$21.00         |
| Yes       | <b>Norethindrone/EE</b> (BREVICON) generic<br>AB-rated to Modicon <sup>®</sup> (0.5mg norethindrone/35mcg EE)   | Watson           | \$52.51                         | \$23.80                    |
| Yes       | ORTHO-NOVUM (1+50) = 1mg norethindrone/ 50mcg mestranol)  | ORTHO            | \$55.33                         | \$22.40                    |
| Yes       | NORINYL 1+50; (AB-rated Brand to Ortho-Novum)   | Watson           | \$50.35                         | \$22.40                    |
| Yes       | <b>Norethindrone/Mestranol</b> (NECON) AB-rated generic   | Watson           | \$29.47                         | \$22.40                    |
| Yes       | LOESTRIN <sup>®</sup> & LOESTRIN FE <sup>®</sup> =<br>1.5 mg norethindrone / EE 30mcg with or without iron<br>1.0 mg norethindrone / EE 20 mcg with or without iron               | Duramed/Barr     | \$55.30                         | \$25.48                    |
| Yes       | Norethindrone acetate/EE (MICROGESTIN & FE)<br>AB rated to LOESTRIN <sup>®</sup> and LOESTRIN FE <sup>®</sup>   | Watson           | \$28.93                         | \$21.84                    |
| Yes       | Norethindrone acetate/EE (JUNEL & FE) generic<br>AB-rated to LOESTRIN <sup>®</sup> and LOESTRIN FE <sup>®</sup>   | Barr             | \$28.94                         | \$21.84                    |
| Yes       | DEMULEN <sup>®</sup> = ethynodiol 1mg / EE 35mcg or EE 50 mcg   | Searle           | \$40.89                         | \$22.68                    |
| Yes       | Ethinodiol/EE (ZOVIA) AB-rated generic  | Watson           | \$29.88                         | \$22.68                    |
| Yes       | Ethinodiol/EE (KELNOR) AB-rated generic   | Barr             | \$29.88                         | \$22.68                    |
| Yes       | LO/OVRAL <sup>®</sup> = norgestrel 0.3mg / 30 mcg EE  | Wyeth            | \$40.84                         | \$23.80                    |
| Yes       | Norgestrel/EE (CRYSSELLE) generic<br>AB-rated to LoOvral <sup>®</sup>   | Barr             | \$30.52                         | \$23.80                    |
| Yes       | Norgestrel/EE (LOW-OGESTREL) AB-rated generic to LoOvral <sup>®</sup>   | Watson           | \$30.52                         | \$23.80                    |
| Yes       | OVRAL <sup>®</sup> = norgestrel 0.5mg / 50mcg EE  | Wyeth            | \$57.56                         | \$31.92                    |
| Yes       | Norgestrel/EE (OGESTREL) AB generic rated to Ovral  | Watson           | \$44.92                         | \$31.92                    |
| Yes       | NORDETTE <sup>®</sup> = levonorgestrel 0.15mg / EE 30 mcg   | Monarch          | \$55.30                         | \$23.52                    |
| No        | LEVLEN <sup>®</sup> 0.15mg levonorgestrel / EE 30 mcg   | Berlex           | \$38.03                         | \$23.52                    |
| Yes       | L-norgestrel/EE (PORTIA) AB-rated generic to Nordette <sup>®</sup>  | Barr             | \$39.93                         | \$23.52                    |
| Yes       | L-norgestrel/EE (LEVORA ) AB-rated generic to Nordette <sup>®</sup>   | Watson           | \$30.93                         | \$23.52                    |
| No        | YASMIN <sup>®</sup> = drospirenone 3mg / EE 30 mcg  | Berlex           | \$49.94                         | --                         |
| No        | YAZ <sup>®</sup> = drospirenone 3mg /EE 20 mcg  | Berlex           | \$49.94                         | --                         |

<sup>a</sup> Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of June 2006 for 1 cycle of therapy.

**TABLE 3: BIPHASIC ORAL CONTRACEPTIVES PRODUCTS (GROUPED BY GENERIC EQUIVALENCY)**

| Preferred | Drug (EE = ethinyl estradiol)   | Mfg     | AWP per cycle <sup>a</sup> | MAC per cycle <sup>a</sup> |
|-----------|---|---------|----------------------------|----------------------------|
| No        | MIRCETTE <sup>®</sup> =<br>desogestrel 0.15mg / 20mcg EE (x 21 days) + 10mcg EE (5 days)                                | Organon | \$50.03                    | \$27.72                    |
| Yes       | <b>Desogestrel/EE</b> (KARIVA) AB-rated generic   | Barr    | \$45.01                    | \$27.72                    |
| Yes       | ORTHO-NOVUM <sup>®</sup> 10/11 =<br>norethindrone 0.5 / 35mcg EE x 10 days<br>+ 1.0 norethindrone / 35 mcg EE (11 days) | Ortho   | \$60.35                    | \$24.36                    |
| Yes       | <b>Norethindrone/EE</b> (NECON) AB-rated generic  | Watson  | \$32.14                    | \$24.36                    |

<sup>a</sup> Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of June 2006 for 1 cycle of therapy.

**TABLE 4: TRIPHASIC ORAL CONTRACEPTIVES PRODUCTS (GROUPED BY GENERIC EQUIVALENCY)**

| Preferred | Drug (EE = ethinyl estradiol)   | Mfg             | AWP per cycle <sup>a</sup> | MAC per cycle <sup>a</sup> |
|-----------|---|-----------------|----------------------------|----------------------------|
| Yes       | TRI-NORINYL <sup>®</sup> = norethindrone (0.5mg, 1mg, 0.5mg) + EE 35mcg   | Watson          | \$50.35                    | \$31.08                    |
| Yes       | Norethindrone/EE (Aranelle) generic<br>AB-rated to Tri-Norinyl  | Barr            | \$39.35                    | \$31.08                    |
|           | Norethindrone/EE (Leena) generic<br>AB-rated to Tri-Norinyl   | Watson          | \$39.35                    | \$31.08                    |
| Yes       | ORTHO-NOVUM <sup>®</sup> 7-7-7<br>= norethindrone (0.5mg, 0.75mg, 1mg) + EE 35 mcg  | Ortho           | \$52.81                    | \$23.24                    |
| Yes       | <b>Norethindrone/EE</b> (NORTREL) generic<br>AB-rated to Ortho-Novum <sup>®</sup> 7-7-7   | Barr            | \$32.23                    | \$23.24                    |
|           | <b>Norethindrone/EE</b> (NECON) generic<br>AB-rated to Ortho-Novum <sup>®</sup> 7-7-7   | Watson          | \$32.20                    | \$23.24                    |
| Yes       | TRI-LEVLEN 28 =<br>Levonorgestrel 0.05mg / 30mcg EE +<br>Levonorgestrel 0.075 mg / 40 mcg EE +<br>Levonorgestrel 0.125mg / 30m cg EE          | Berlex          | \$36.34                    | \$20.44                    |
| Yes       | TRIPHASIL <sup>®</sup> =<br>Levonorgestrel 0.05mg / 30mcg EE +<br>Levonorgestrel 0.075 mg / 40 mcg EE +<br>Levonorgestrel 0.125mg / 30m cg EE | Wyeth           | \$36.88                    | \$20.44                    |
| Yes       | <b>Levonorgestrel/EE</b> (TRIVORA) generic<br>AB-rated to Triphasil <sup>®</sup> , Tri-Levlen <sup>®</sup>                                    | Watson          | \$27.49                    | \$20.44                    |
| Yes       | <b>Levonorgestrel/EE</b> (ENPRESSE) generic<br>AB-rated to Triphasil <sup>®</sup> , Tri-Levlen <sup>®</sup>                                   | Duramed/Barr    | \$27.49                    | \$20.44                    |
| Yes       | ORTHO TRI-CYCLEN <sup>®</sup> =<br>Norgestimate (0.18mg, 0.215mg, 0.25mg) + EE 35mcg  | Ortho           | \$48.08                    | \$25.76                    |
| Yes       | <b>Norgestimate/EE</b> (TRI-SPRINTEC)<br>AB-rated generic to Ortho Tri-Cyclen <sup>®</sup>  | Barr            | \$39.32                    | \$25.76                    |
| Yes       | <b>Norgestimate/EE</b> (TRINESSA)<br>AB-rated generic to Ortho Tri-Cyclen <sup>®</sup>  | Watson          | \$39.32                    | \$25.76                    |
| Yes       | <b>Norgestimate/EE</b> (TRI-PREVIFEM)<br>AB-rated generic to Ortho Tri-Cyclen <sup>®</sup>  | Teva            | \$39.32                    | \$25.76                    |
| Yes       | ORTHO TRI-CYCLEN <sup>®</sup> LO =<br>Norgestimate (0.18mg, 0.215mg, 0.25mg) + EE 25 mcg  | Ortho           | \$52.41                    | --                         |
| Yes       | ESTROSTEP <sup>®</sup> FE = norethindrone 1mg + EE 20-30-35 mcg + Fe 75mg   | Warner-Chilcott | \$47.68                    | --                         |
| No        | CYCLESSA <sup>®</sup> = desogestrel 0.10 – 0.125 – 0.150 mg + EE 25 mcg   | Organon         | \$45.29                    | \$25.48                    |
| Yes       | <b>Desogestrel/EE</b> (VELIVET)   | Barr            | \$33.64                    | \$25.48                    |

<sup>a</sup> Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of June 2006 for 1 cycle of therapy.

**TABLE 5: OTHER CONTRACEPTIVE PRODUCTS: RINGS/PATCHES**

| Preferred | Drug   | Mfg    | AWP per cycle <sup>a</sup> | MAC per cycle <sup>a</sup> |
|-----------|--|--------|----------------------------|----------------------------|
| Yes       | NuvaRing <sup>®</sup> = three month ring provides<br>etonogestrel 1.2mg + 15mcg EE per day     | Ortho  | \$45.74                    | --                         |
| Yes       | OrthoEvra <sup>®</sup> = weekly patch provides<br>norelgestromin 0.15 mg and EE 20 mcg per day | Watson | \$53.89                    | --                         |

<sup>a</sup> Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of June 2006 for 1 cycle of therapy

**TABLE 6: PROGESTIN ONLY ORAL CONTRACEPTIVE PRODUCTS (GROUPED BY GENERIC EQUIVALENCY)**

| Preferred | Drug   | Mfg    | AWP per cycle <sup>a</sup> | MAC per cycle <sup>a</sup> |
|-----------|--|--------|----------------------------|----------------------------|
| Yes       | ORTHO MICRONOR <sup>®</sup> = norethindrone 0.35mg   | Ortho  | \$64.25                    | \$25.20                    |
| Yes       | <b>Norethindrone 0.35mg (ERRIN) generic</b><br>AB-rated to Ortho-Micronor <sup>®</sup>                         | Barr   | \$36.92                    | \$25.20                    |
| Yes       | <b>Norethindrone 0.35mg (JOLIVETTE) generic</b><br>AB-rated to Ortho-Micronor <sup>®</sup>                     | Watson | \$36.92                    | \$25.20                    |
| Yes       | NOR-Q-D <sup>®</sup> = norethindrone 0.35mg  | Watson | \$55.91                    | \$25.20                    |
| Yes       | <b>Norethindrone 0.35mg (NORA-BE<sup>®</sup>)</b><br><b>(Holds same NDA as NOR-QD) - recognized as generic</b> | Watson | \$36.92                    | \$25.20                    |
| Yes       | <b>Norethindrone 0.35mg (CAMILA) generic</b><br>AB-rated to Nor-QD <sup>®</sup>                                | Barr   | \$36.92                    | \$25.20                    |
| Yes       | OVRETTE = norgestrel 0.075 mg  | Wyeth  | \$39.10                    | --                         |

<sup>a</sup>Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of June 2006 for 1 cycle of therapy.

**TABLE 7: EMERGENCY CONTRACEPTIVE PRODUCTS**

| Preferred | Drug                           | Mfg          | AWP per cycle <sup>a</sup> | MAC per cycle <sup>a</sup> |
|-----------|--------------------------------|--------------|----------------------------|----------------------------|
| Yes       | PLAN B = levonorgestrel 0.75mg | Duramed/Barr | \$31.77                    | --                         |

<sup>a</sup>Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of June 2006 for 1 cycle of therapy.

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